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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/835,523	04/17/2001	Yong-Qian Wu	23754X	5679
29728	7590	01/06/2006	EXAMINER	
GUILFORD PHARMACEUTICALS C/O FOLEY & LARDNER LLP 3000 K STREET, NW WASHINGTON, DC 20007-5143			TRUONG, TAMTHOM NGO	
			ART UNIT	PAPER NUMBER
			1624	

DATE MAILED: 01/06/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/835,523

Applicant(s)

WU ET AL.

Examiner

Tamthom N. Truong

Art Unit

1624

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 09 December 2005.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-40 and 48-51 is/are pending in the application.
- 4a) Of the above claim(s) 5,6,11-40 and 49-51 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1,2,4,7-10 and 48 is/are rejected.
- 7) ☒ Claim(s) 3 is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- ☒ Notice of References Cited (PTO-892)
- ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____
- ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____
- ☐ Notice of Informal Patent Application (PTO-152)
- ☐ Other: _____

NON-FINAL ACTION

Applicant's amendment of 12-9-05 has been fully considered. Applicant's terminal disclaimer has overcome the previous rejection of ODP, and thus, said rejection is withdrawn herein.

An update search yields a relevant reference which necessitates a new ground of rejection. Therefore, finality is withdrawn herein.

Claims 1-40 and 48-51 are pending.

Claims 5, 6, 11-40, and 49-51 are withdrawn.

Claims 1-4, 7-10 and 48 remain for consideration.

Claim Rejections - 35 USC § 112, First Paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

1. **Scope of Enablement:** Claims 7 and 10 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the treatment of *peripheral neuropathy*, does not reasonably provide enablement for the treatment of *Alzheimer's disease, Parkinson's disease, Huntington's disease or amyotrophic lateral sclerosis*. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

Although the scope of claims 7 and 10 have been amended, they still recite the treatment of many neurological diseases that have different manifestations and etiologies. For example, Alzheimer's disease is related to acetylcholine while Parkinson's disease is related to dopamine, and Huntington's disease does not have a known cause.

The specification does not provide a correlation between treating the above diseases with the biological activity of the claimed compounds.

The state of the art does not support the treatment of those neurological diseases as evident by **Jacobson** (US'014 & US'670 – cited previously) and **Sugimura et. al.** (US'908 – cited previously).

Thus, with the unpredictable nature of the pharmaceutical art, the skilled clinician would have to engage in undue experimentation to treat the many neurological diseases recited in claims 7 and 10.

Claim Rejections - 35 USC § 112, Second Paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

2. Claims 1, 2, 4, 7-10 and 48 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

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Claims 1 and 7 recite the definition of R_1 which includes “ $-CR_3$ ” which has indefinite metes and bounds because there is no definition for “R”. If variable “ R_3 ” is intended, then there is incomplete valence for “ $-CR_3$ ”.

Claims 2-4, 8-10 and 48 are rejected as being dependent on either claim 7 or 10, and carrying out the indefinite limitations.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

3. Claims 1, 2, 4 and 48 are rejected under 35 U.S.C. 103(a) as being unpatentable over **Casini et. al.** (EP 572,365 A2).

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

On page 3, Casini et. al. disclose formula IV which includes many pyrazolyl derivatives that generically encompasses many compounds of the instant formula I with the following substituents:

- i. R_1 is $-CR_3$;
- ii. R_3 is an alkyl group substituted with a carboxy group;
- iii. X is O;
- iv. $n = 1$;
- v. R_2 is an alkyl chain.

Note, variables of formula IV only represent a few moieties, which provides equivalent teaching sufficiently to motivate the skilled chemist to select the *pyrazolyl derivatives*, particularly when the disclosed variables represent the following moieties:

- i. X_1 and X_2 are $-CH_2$ groups; R is hydrogen;
- ii. X_3 and X_4 are N atoms (i.e. pyrazolyl);
- iii. R_1 and R_3 are $-CH_2$ groups; $n = 0$ (this side chain corresponds to the instant R_1 as $-CR_3$);
- iv. R_2 and R_4 represent CO groups;
- v. R_5 and R_6 represent $-CH_2$ groups (this side chain corresponds to the instant R_2);

The disclosed formula IV has activity on smooth muscle and inhibit thrombocytes aggregation. Therefore, given the narrow scope of formula IV, it would have been within the level of the skilled chemist to select pyrazolyl compounds claimed herein for pharmaceutical use.

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Thus, at the time that the invention was made, it would have been obvious to make and use pyrazolyl compounds of the instant formula I in view of the teaching above.

Claim Objections

4. Claim 3 is objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.


Claim 3 is free of prior art because it recites pyrazolyl species substituted with an 'alkanoyl' group that is not taught or fairly suggested by the prior art of record.

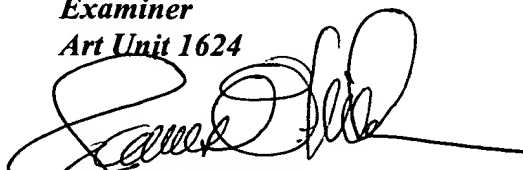
Any inquiry concerning this communication or earlier communications from the examiner should be directed to Tamthom N. Truong whose telephone number is 571-272-0676. The examiner can normally be reached on M-F (9:30-6:00).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James O. Wilson can be reached on 571-272-0661. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

12-24-05


Tamthom N. Truong
Examiner
Art Unit 1624


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